REMARKS

Claims 4-7 are pending in this application. Claims 1-3 have been rejected.

Claims 1-3 have been canceled without prejudice or disclaimer, and have been rewritten as new claims 4-7 to more clearly define the invention. Claims 4-7 find support throughout the specification and claims as filed. No new matter has been added.

In view of new claims 4-7 and the remarks set forth below, further and favorable consideration is respectfully requested.

1. ***At page 2, paragraph 2, of the Office Action, claims 1-3, have been rejected under 35 USC § 103(a), as being unpatentable over Anazawa et al. (US Patent No: 5,192,320) in view of Kashiwabara et al (EP-1057492) and Motomura et al. (EP-0769503).***

The Examiner states that it would have been obvious to the skilled artisan, to add Kashiwabara's coating to the blood contacting side of the membrane in Anazawa's device for the purpose of importing anti-thrombogenic properties thereto, and that it would have been obvious to use dimethyl dioctadecyl ammonium salt in place of dimethyl ditetradecyl ammonium salt in Kashiwabara's product and process given Motomura's teaching that they are known equivalents for this purpose and would result in predictable variations in the lifetime of the coating, capability of the coating, etc. A brief analysis of Anazawa, Kashiwabara and Motomura, is set forth below.

Anazawa is directed to an artificial lung and a method of using it. The artificial lung performs the exchange of gases between blood and a gas through a homogeneous membrane by passing blood over one side of the membrane and oxygen over the other side. The membrane is a

hollow fiber membrane composed of polyolefin and has an oxygen flux of at least 1 x 10^{-6}(cm^3(STP)/(cm^2.sec.cmHg)). The membrane has an ethanol flux of not more than 30 ml/(min.m^2).

Anazawa teaches at col. 2, lines 14-49, that composite membranes obtained by coating or "clogging" a compound on the hollow fiber membrane, are ***undesirable*** because the treatment required is complex, presents many technical problems including difficulty in controlling: the thickness of the clogging layer, the strength of the membrane, and pinhole formation. Anazawa also discloses that such composite membranes are high in price given their low productivity. Anazawa states that homogenous membrane-type artificial lungs are advantageous.

Kashiwabara is directed to a blood compatible composition and medical device using the composition. The composition includes an ionic complex consisting of an organic cationic compound and heparin or a derivative thereof, where the organic cationic compound is an ammonium or a phosophonium bound with four aliphatic alkyl groups having a total number of carbon atoms of 24 to 32, and having at least 2 alkyl groups having not less than 10 carbon atoms.

Kashiwabara discloses a medical device capable of long-term, sustained, antithrombogenicity achieved by coating the surface of the device with the composition.

Motomura is directed to a heparin complex and a medical device coated with the complex. The complex of Motomura is a cationic alkyldimethylammonium and heparin, which complex does not substantially dissolve in blood. Suitable cationic ammonium salts are disclosed on page 3 of Motomura.

In view of the following, this rejection is respectfully overcome.

Claims 1-3 have been canceled without prejudice or disclaimer and have been rewritten as new claims 4-7 to more clearly define the invention. No new matter has been added.

It is submitted that the combination of Anazawa with Kashiwabara and/or Motomura, is improper because there is no motivation, suggestion or incentive supporting the combination.

Specifically, Anazawa requires a homogenous membrane. Anazawa ***teaches away*** from composite membranes, i.e., membranes coated or impregnated with a composition. Thus, the skilled artisan in view of Anazawa directed to homogenous membranes, would have no motivation to look to art directed to coating compositions, i.e., Kashiwabara and Motomura. Likewise, the skilled artisan in view of Kashiwabara and/or Motomura directed to coating compositions for medical devices, would have no motivation to look to art requiring an uncoated device, i.e., Anazawa.

Assuming *arguendo* the combination proper, none of the applied references taken alone or together, suggest the presently claimed invention. None of the references suggest providing a gas exchange membrane with a coating to prevent clot formation. In fact, Anazawa, ***teaches away*** from a coated membrane.

Present claim 1 requires an ionic complex containing both a quaternary aliphatic alkylammonium salt having from 22 to 26 carbon atoms and a quaternary aliphatic alkylammonium salt having from 37 to 40 carbon atoms, and heparin. The present specification teaches at the paragraph bridging pages 15 and 16, that the invention achieves "more adequate" anti-thrombotic properties, than can be achieved using an ammonium salt of a single structure with heparin.

None of the applied references teach or suggest a complex including both a quaternary aliphatic alkylammonium salt having from 22 to 26 carbon atoms and a quaternary aliphatic alkylammonium salt having from 37 to 40 carbon atoms, as presently required.

Kashiwabara discloses a quaternary aliphatic alkylammonium salt having from 24 to 32 carbon atoms in the alkyl group, and does not disclose or suggest the quaternary aliphatic alkylammonium salt having from 37 to 40 carbon atoms, as required in the present invention.

Motomura does not disclose or suggest the combined use of the specific alkylammonium salts as required in the present invention, i.e., a first quaternary aliphatic alkylammonium salt having from 22 to 26 carbon atoms in total and a second quaternary aliphatic alkylammonium salt having from 37 to 40 carbon atoms in total. Even if such a combined use were suggested therein, Motomura merely discloses an ionic complex of dimethylalkylammonium salt-heparin, whereas the ionic complex for use in the present invention has a structure of aliphatic alkylammonium salt-heparin-aliphatic alkylammonium salt.

None of the cited references disclose any method of coating an anti-thrombotic material to a membrane artificial lung. Rather, Anazawa ***teaches away*** from a coated membrane at col. 2, line 14-49.

In view of new claims 4-7, and the remarks set forth above, it is submitted that a *prima facie* case of obviousness has not been established. Further, it is submitted that nothing in any of the references applied by the Examiner, taken alone or together, renders the claimed invention obvious within the meaning of 35 USC § 103. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

If, for any reason, it is felt that this application is not now in condition for allowance, the Examiner is requested to contact Applicants undersigned attorney at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.

In the event that this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

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